Devi, S.
09/120044

- key terms

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     FILE 'CAPLUS' ENTERED AT 15:55:19 ON 02 SEP 1999
L1          2901 SEA ABB=ON  PLU=ON  PNEUMOLYS? OR PNEUMOCOC?
L2            95 SEA ABB=ON  PLU=ON  L1 AND MODIF?
L3            26 SEA ABB=ON  PLU=ON  L2 AND (MUTAT? OR MUTANT OR MUTAGEN?
                 OR POLYMORPH? OR POLY MORPH?)

=> d 1-26 .beverly

L3   ANSWER 1 OF 26  CAPLUS  COPYRIGHT 1999 ACS
ACCESSION NUMBER:         1999:187746  CAPLUS
DOCUMENT NUMBER:          131:29594
TITLE:                    Penicillin-binding protein-mediated resistance
                          in pneumococci and staphylococci
AUTHOR(S):                Chambers, Henry F.
CORPORATE SOURCE:         Medical Service, San Francisco General Hospital,
                          and Department of Medicine, University of
                          California, San Francisco, CA, 94143, USA
SOURCE:                   J. Infect. Dis. (1999), 179(Suppl. 2), S353-S359
                          CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER:                University of Chicago Press
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review with 58 refs. Target alteration underlies resistance to
     .beta.-lactam antibiotics in both Staphylococcus species and
     Streptococcus pneumoniae. The penicillin-binding protein (PBP)
     targets in penicillin-resistant strains of S. pneumoniae are
     modified, low-binding-affinity versions of the native PBPs.
     Multiple PBP targets may be modified by transformation and
     homologous recombination with DNA from PBP genes of viridans
     streptococci. The level of resistance is detd. by how many and to
     what extent targets are modified. In contrast,
     methicillin resistance in staphylococci is due to expression of PBP
     2a, a novel, low-affinity PBP for which there is no homolog in
     methicillin-susceptible strains. PBP 2a is encoded by mecA, a
     highly conserved gene most likely acquired by a rare transposition
     from Staphylococcus sciuri or a closely related ancestor.
     Expression of resistance can be highly variable, but this seems not
     to be detd. by PBP modifications. Several non-PBP factors
     are required for high-level resistance.

L3   ANSWER 2 OF 26  CAPLUS  COPYRIGHT 1999 ACS
ACCESSION NUMBER:         1999:77590  CAPLUS
DOCUMENT NUMBER:          130:152551
TITLE:                    Modified immunogenic
                          pneumolysin compositions as vaccines
INVENTOR(S):              Minetti, Conceicao; Michon, Francis; Pullen,
                          Jeffrey K.; Polvino-Bodnar, Maryellen; Liang,
                          Shu-Mei; Tai, Joseph Y.
PATENT ASSIGNEE(S):       North American Vaccine, Inc., USA
                             Searcher  :  Shears  308-4994
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SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9903884	A2	19990128	WO 1998-US14716	19980721
WO 9903884	A3	19990408		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9884078	A1	19990210	AU 1998-84078	19980721
PRIORITY APPLN. INFO.:			US 1997-53306	19970721
			US 1998-73456	19980202
			US 1998-345697	19980202
			WO 1998-US14716	19980721

AB This invention relates to **modified pneumolysin** polypeptides that retain the immunogenic nature of **pneumolysin** but have reduced or undetectable hemolytic activity compared to native **pneumolysin**. The invention also provides a method for generating novel **pneumolysin** variants with these desired characteristic properties. The invention also provides immunogenic compns. useful as pharmaceutical compns. including vaccines in which non-toxic, **modified pneumolysin** is used to stimulate protective immunity against Streptococcus pneumoniae. The vaccines may be compns. in which the **modified pneumolysin** in conjugated to bacterial polysaccharides or may be carried on an attenuated viral vector. In addn., the invention also provides a method of using the non-toxic, **modified pneumolysin** toxoid in order to stimulate antibodies against Streptococcus pneumoniae in a treated individual which are then isolated and transferred to a second individual, thereby conferring protection against Streptococcus pneumoniae in the second individual. Prepd. and tested for immunogenicity were polypeptides pNVJ1, pNVJ20, pNVJ22, pNVJ45, pNVJ56, pNVJ103, pNVJ207, pNVJ111, and pNVJ211 and corresponding nucleic acid sequences.

L3 ANSWER 3 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1998:783992 CAPLUS
Searcher : Shears 308-4994

DOCUMENT NUMBER: 130:120724
TITLE: The molecular mechanism of **pneumolysin**, a virulence factor from Streptococcus pneumoniae
AUTHOR(S): Rossjohn, Jamie; Gilbert, Robert J. C.; Crane, Dennis; Morgan, Peter J.; Mitchell, Timothy J.; Rowe, Arthur J.; Andrew, Peter W.; Paton, James C.; Tweten, Rodney K.; Parker, Michael W.
CORPORATE SOURCE: The Ian Potter Foundation Protein Crystallography Laboratory, St. Vincent's Institute of Medical Research, Fitzroy, 3065, Australia
SOURCE: J. Mol. Biol. (1998), 284(2), 449-461
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Pneumolysin**, a member of the thiol-activated cytolysin family of toxins, is a virulence factor from the Gram-pos. bacterium Streptococcus pneumoniae. The toxin forms large oligomeric pores in cholesterol-contg. membranes of eukaryotic cells. A plethora of biochem. and **mutagenesis** data have been published on **pneumolysin**, since its initial characterization in the 1930s. Here we present an homol. model of the monomeric and oligomeric forms of **pneumolysin** based on the recently detd. crystal structure of perfringolysin O and electron microscopy data. A feature of the model is a striking electroneg. surface on parts of **pneumolysin** that may reflect its cytosolic location in the bacterial cell. The models provide a mol. basis for understanding the effects of published **mutagenesis** and biochem. **modifications** on the toxic activity of **pneumolysin**. In addn., spectroscopic data are presented that shed new light on **pneumolysin** activity and have guided us to hypothesize a detailed model of membrane insertion. These data show that the environment of some tryptophan residues changes on insertion and/or pore formation. In particular, spectroscopic anal. of a tryptophan **mutant**, W433F, suggests it is the residue mainly responsible for the obsd. effects. Furthermore, there is no change in the secondary structure content when the toxin inserts into membranes. Finally, the basis of the very low activity shown by a **pneumolysin** mol. from another strain of S. pneumoniae may be due to the movements of a key domain-domain interface. The mol. basis of **pneumolysin** -induced complement activation may be related to the structural similarity of one of the domains of **pneumolysin** to Fc, rather than the presumed homol. of the toxin to C-reactive protein as previously suggested. (c) 1998 Academic Press.

L3 ANSWER 4 OF 26 CAPLUS
Searcher : Shears 308-4994

ACCESSION NUMBER: 1998:122808 CAPLUS
DOCUMENT NUMBER: 128:240572
TITLE: A conserved tryptophan in **pneumolysin** is a determinant of the characteristics of channels formed by **pneumolysin** in cells and planar lipid bilayers
AUTHOR(S): Korchev, Yuri E.; Bashford, C. Lindsay; Pederzolli, Cecilia; Pasternak, Charles A.; Morgan, Peter J.; Andrew, Peter W.; Mitchell, Timothy J.
CORPORATE SOURCE: Department of Cellular and Molecular Sciences, St. George's Hospital Medical School, London, SW17 0RE, UK
SOURCE: Biochem. J. (1998), 329(3), 571-577
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Pneumolysin** is one of the family of thiol-activatable, cytolytic toxins. Within these toxins the amino acid sequence Trp-Glu-Trp-Trp is conserved. **Mutations** made in this region of **pneumolysin**, residues 433-436 inclusive, did not affect cell binding or the formation of toxin oligomers in the target cell membrane. However, the **mutations** did affect hemolysis, leakage of low-mol.-mass metabolites from Lettre cells and the induction of conductance channels across planar lipid bilayers. Of eight **modified pneumolysins** examd., Trp-433 .fwdarw. Phe showed the smallest amt. of hemolysis or leakage (less than 5% of wild type). **Pneumolysin** -induced leakage from Lettre cells was sensitive to inhibition by bivalent cations but the extent of inhibition varied depending on the **modification**. Leakage by the **mutant** Trp-433 .fwdarw. Phe was least sensitive to cation inhibition. The ion-conducting channels formed across planar lipid bilayers exhibit small (less than 30 pS), medium (30 pS-1 nS) and large (more than 1 nS) conductance steps. Small- and medium-sized channels were preferentially closed by bivalent cations. In contrast with wild-type toxin, which formed predominantly small channels, the **modified** toxin Trp-433 .fwdarw. Phe formed large channels that were insensitive to cation-induced closure. Polysaccharides of mol. mass more than 15 kDa inhibited hemolysis by wild-type toxin, but polysaccharide of up to 40 kDa did not prevent hemolysis by Trp-433 .fwdarw. Phe. Electron microscopy revealed that Trp-433 .fwdarw. Phe formed oligomeric arc and ring structures with dimensions identical with those of wild-type toxin, and that the ratio of arcs to rings formed was the same for wild-type toxin and the Trp-433 .fwdarw. Phe variant. We conclude that the change Trp-433 .fwdarw. Phe affects channel formation at a point subsequent to binding to the cell membrane and the formation of oligomers, and

that the size of arc and ring structures revealed by electron microscopy does not reflect the functional state of the channels.

L3 ANSWER 5 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:201910 CAPLUS
DOCUMENT NUMBER: 124:255575
TITLE: In vitro activities of U-100592 and U-100766, novel oxazolidinone antibacterial agents
AUTHOR(S): Zurenko, Gary E.; Yagi, Betty H.; Schaadt, Ronda D.; Allison, John W.; Kilburn, James O.; Glickman, Suzanne E.; Hutchinson, Douglas K.; Barbachyn, Michael R.; Brickner, Steven J.
CORPORATE SOURCE: Pharmacia & Upjohn, Inc., Kalamazoo, MI, 49001, USA
SOURCE: Antimicrob. Agents Chemother. (1996), 40(4), 839-45
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Oxazolidinones make up a relatively new class of antimicrobial agents which possess a unique mechanism of bacterial protein synthesis inhibition. U-100592 {(S)-N-[[3-[3-fluoro-4-[4-(hydroxyacetyl)-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide} and U-100766 {(S)-N-[[3-[3-fluoro-4-(4-morpholinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide} are novel oxazolidinone analogs from a directed chem. **modification** program. MICs were detd. for a variety of bacterial clin. isolates; the resp. MICs of U-100592 and U-100766 at which 90% of isolates are inhibited were as follows: methicillin-susceptible Staphylococcus aureus, 4 and 4 .mu.g/mL; methicillin-resistant S. aureus, 4 and 4 .mu.g/mL; methicillin-susceptible Staphylococcus epidermidis, 2 and 2 .mu.g/mL; methicillin-resistant S. epidermidis, 1 and 2 .mu.g/mL; Enterococcus faecalis, 2 and 4 .mu.g/mL; Enterococcus faecium, 2 and 4 .mu.g/mL; Streptococcus pyogenes, 1 and 2 .mu.g/mL; Streptococcus pneumoniae, 0.50 and 1 .mu.g/mL; Corynebacterium spp., 0.50 and 0.50 .mu.g/mL; Moraxella catarrhalis, 4 and 4 .mu.g/mL; Listeria monocytogenes, 8 and 2 .mu.g/mL; and Bacteroides fragilis, 16 and 4 .mu.g/mL. Most strains of Mycobacterium tuberculosis and the gram-pos. anaerobes were inhibited in the range of 0.50 to 2 .mu.g/mL. Enterococcal strains resistant to vancomycin (VanA, VanB, and VanC resistance phenotypes), **pneumococcal** strains resistant to penicillin, and M. tuberculosis strains resistant to common antitubercular agents (isoniazid, streptomycin, rifampin, ethionamide, and ethambutol) were not cross-resistant to the oxazolidinones. The presence of 10, 20, and 40% pooled human serum did not affect the antibacterial activities of the oxazolidinones. Time-kill studies demonstrated a bacteriostatic effect of the analogs against staphylococci and enterococci but a bactericidal

effect against streptococci. The spontaneous **mutation** frequencies of S. aureus ATCC 29213 were <3.8 .times. 10-10 and <8 .times. 10-11 for U-100592 and U-100766, resp. Serial transfer of three staphylococcal and two enterococcal strains on drug gradient plates produced no evidence of rapid resistance development. Thus, these new oxazolidinone analogs demonstrated in vitro antibacterial activities against a variety of clin. important human pathogens.

L3 ANSWER 6 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1993:488721 CAPLUS
DOCUMENT NUMBER: 119:88721
TITLE: Ethanol impairs neutrophil chemotaxis in vitro but not adherence or recruitment to lungs of rats with experimental **pneumococcal** pneumonia
AUTHOR(S): Lister, Philip D.; Gentry, Martha J.; Preheim, Laurel C.
CORPORATE SOURCE: Sect. Infect. Dis., VA Med. Cent., Omaha, NE, USA
SOURCE: J. Infect. Dis. (1993), 167(5), 1131-7
CODEN: JIDIAQ; ISSN: 0022-1899
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of 7 days of ethanol ingestion on circulating neutrophil (PMNL) counts and PMNL adherence, chemotaxis, and recruitment was investigated. Pair-feeding of rats resulted in a significant decrease in PMNL counts in both ethanol-fed and control rats. The mean no. of PMNL exhibiting chemotaxis in a **modified** Boyden chamber in response to lipopolysaccharide-activated normal rat serum was significantly decreased in ethanol-fed rats compared with controls. The percentage of adherence to nylon wool columns, however, was similar in both groups. To measure pulmonary PMNL recruitment, rats were infected transtracheally with 105 Streptococcus pneumoniae and sacrificed. Bronchoalveolar lavage fluid from both groups contained similar nos. of PMNL 8 h after infection. By 24 h, PMNL nos. in lavage fluid from ethanol-fed rats exceeded those in controls. PMNL recruitment continued in the ethanol-fed rats at 48 and 72 h, whereas values in controls had returned to baseline. Thus, the impaired pulmonary defense against S. pneumoniae in ethanol-fed rats is not due to defective PMNL recruitment.

L3 ANSWER 7 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1992:509828 CAPLUS
DOCUMENT NUMBER: 117:109828
TITLE: Comparative efficacy of autolysin and **pneumolysin** as immunogens protecting mice against infection by Streptococcus pneumoniae

AUTHOR(S): Lock, Robert A.; Hansman, David; Paton, James C.
CORPORATE SOURCE: Dep. Microbiol., Adelaide Child. Hosp., North Adelaide, Australia
SOURCE: Microb. Pathog. (1992), 12(2), 137-43
CODEN: MIPAEV; ISSN: 0882-4010
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous studies on S. pneumoniae have established that the **pneumococcal** proteins autolysin (N-acetylmuramyl-L-alanine amidase) and **pneumolysin** both contribute significantly to the virulence of the organism. Here, autolysin and a defined toxoid deriv. of **pneumolysin** were tested, individually and in combination, for efficacy in a mouse model as antigens protecting against challenge with virulent, wild-type S. pneumoniae. While each antigen alone provided significant protection, the degree of protection was not increased when the antigens were administered together. In an addnl. expt., mice were challenged with a genetically-**modified mutant** strain of **pneumococcus** unable to express active **pneumolysin**. Pre-immunization of such mice with autolysin failed to provide any significant protection against the challenge. Apparently, the most important contribution made by autolysin to the virulence of S. pneumoniae may be its role in mediating the release of **pneumolysin** from the **pneumococcal** cytoplasm during infection.

L3 ANSWER 8 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1992:122142 CAPLUS
DOCUMENT NUMBER: 116:122142
TITLE: Characterization and sequence of the Escherichia coli stress-induced psp operon
AUTHOR(S): Brissette, Janice L.; Weiner, Lorin; Ripmaster, Tracy L.; Model, Peter
CORPORATE SOURCE: Rockefeller Univ., New York, NY, 10021, USA
SOURCE: J. Mol. Biol. (1991), 220(1), 35-48
CODEN: JMOBAK; ISSN: 0022-2836
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new E. coli operon, the phage shock protein (psp) operon, is induced in response to heat, ethanol, osmotic shock and infection by filamentous bacteriophages. The operon includes at least four genes: pspA, B, C and E. PspA assocs. with the inner membrane and has the heptad repeats characteristic of proteins that can form coiled coils. The operon encodes a factor that activates psp expression, and deletion analyses indicate that this protein is PspC; PspC is predicted to possess a leucine zipper, a motif present in many eukaryotic transcription factors. The pspE gene is expressed in response to stress as part of the operon, but is also transcribed from its own promoter under normal conditions. In vitro

studies suggest that PspA and C are **modified** in vivo. Expression of the psp genes does not require the heat shock sigma factor, .sigma.32. The increased duration of psp induction in a .sigma.32 **mutant** suggests that a product (or products) of the heat shock response down-regulates expression of the operon.

L3 ANSWER 9 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1992:103557 CAPLUS
DOCUMENT NUMBER: 116:103557
TITLE: **Pneumolysin** induces the salient histologic features of **pneumococcal** infection in the rat lung in vivo
AUTHOR(S): Feldman, C.; Munro, N. C.; Jeffery, P. K.; Mitchell, T. J.; Andrew, P. W.; Boulnois, G. J.; Guerreiro, D.; Rohde, J. A. L.; Todd, H. C.; et al.
CORPORATE SOURCE: Dep. Thorac. Med., Natl. Heart Lung Inst., London, SW3 6LR, UK
SOURCE: Am. J. Respir. Cell Mol. Biol. (1991), 5(5), 416-23
CODEN: AJRBEL; ISSN: 1044-1549
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Streptococcus pneumoniae infections are common, but how they cause host tissue injury and death is incompletely understood. Immunization with **pneumolysin**, a thiol-activated toxin produced by the **pneumococcus**, partially protects animals during subsequent infection. The mechanism by which **pneumolysin** contributes to disease is not known. The aim of the present investigation was to det. the hitol. changes induced by recombinant **pneumolysin** in the rat lung and to compare them with the changes induced by live organisms. Injection of either toxin (200 or 800 ng) or bacteria into the apical lobe bronchus was assocd. with the development of a severe lobar pneumonia restricted to the apical lobe. The changes induced by the toxin were greater at the higher concn., and changes were most severe in those animals in which there was partial ligation of the apical lobe bronchus. The pneumonitis was less severe following injection of a **modified** toxin with decreased hemolytic activity, generated by site-directed **mutagenesis** of the cloned **pneumolysin** gene, indicating that this property of the toxin was important in generating pulmonary inflammation. There was still considerable pneumonitis after injection of a **modified** toxin with decreased capacity to activate complement.

L3 ANSWER 10 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1992:77475 CAPLUS
DOCUMENT NUMBER: 116:77475

TITLE: Truncated forms of PspA that are secreted from Streptococcus pneumoniae and their use in functional studies and cloning of the pspA gene
AUTHOR(S): Yother, Janet; Handsome, Geraline L.; Briles, David E.
CORPORATE SOURCE: Dep. Microbiol., Univ. Alabama, Birmingham, AL, 35294, USA
SOURCE: J. Bacteriol. (1992), 174(2), 610-18
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Insertion-duplication **mutagenesis** was used to generate **mutants** of S. pneumoniae that produced truncated forms of PspA (**pneumococcal** surface protein A). The truncated products, representing from 20 to 80% of the complete PspA mol., were all secreted from the cell and could be detected in unconcd. culture medium. Anal. of the truncated mols. showed that the antigenic variability known to be assocd. with PspA is located in the .alpha.-helical N-terminal half of the mol. This region was also found to contain immunogenic and protection-eliciting epitopes and to define the max. region of the mol. that is likely to be surface exposed. The apparent mol. wt. variability seen for PspA mols. of different S. pneumoniae strains was localized to both the N- and C-terminal halves of the protein. Attachment of PspA to S. pneumoniae was found to require regions located carboxy to the 5th repeat unit in the C-terminal end of the mol. From the insertion-duplication **mutants**, the complete pspA gene was cloned and expressed in Escherichia coli. Differences in apparent mol. wt. were obsd. when the same cloned product was expressed in E. coli and S. pneumoniae, suggesting that PspA is **modified** differently in the 2 hosts.

L3 ANSWER 11 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1991:654020 CAPLUS
DOCUMENT NUMBER: 115:254020
TITLE: Complement activation and antibody binding by **pneumolysin** via a region of the toxin homologous to a human acute-phase protein
AUTHOR(S): Mitchell, T. J.; Andrew, P. W.; Saunders, F. K.; Smith, A. N.; Boulnois, G. J.
CORPORATE SOURCE: Dep. Microbiol., Univ. Leicester, Leicester, LE1 9NH, UK
SOURCE: Mol. Microbiol. (1991), 5(8), 1883-8
CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Pneumolysin**, a membrane-damaging toxin, is known to activate the classical complement pathway. It was shown that 1 .mu.g mL-1 of penumolysin can activate complement, which is a much

lower level than obsd. previously. Two distinct regions of **pneumolysin** were identified which show homol. with a contiguous sequence within acute-phase proteins, including human C-reactive protein (CRP). Site-directed **mutagenesis** of the **pneumolysin** gene was used to change residues common to **pneumolysin** and CRP. Some of the **modified** toxins had a reduced ability both to activate complement and bind antibody. It is suggested that the ability of **pneumolysin** to activate complement is related to its ability to bind the Fc portion of IgG.

L3 ANSWER 12 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1989:528664 CAPLUS
DOCUMENT NUMBER: 111:128664
TITLE: **Pneumolysin**, the thiol-activated toxin of Streptococcus pneumoniae, does not require a thiol group for in vitro activity
AUTHOR(S): Saunders, F. K.; Mitchell, T. J.; Walker, J. A.; Andrew, P. W.; Boulnois, G. J.
CORPORATE SOURCE: Dep. Microbiol., Univ. Leicester, Leicester, LE1 9HN, UK
SOURCE: Infect. Immun. (1989), 57(8), 2547-52
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of the single cysteine residue in the activity of the thiol-activated toxin **pneumolysin** was investigated using oligonucleotide-mediated, site-directed **mutagenesis**. Three **modified** toxins in which the cysteine residue was changed in an alanine, a serine, or a glycine residue were purified to homogeneity and examd. for activity. The Cys-428.fwdarw.Ala **modified** toxin was indistinguishable from the wild-type recombinant toxin in terms of hemolytic activity and lytic and inhibitory effects on human **polymorphonuclear** leukocytes (PMN), indicating that the cysteine residue is not essential for toxin activity. The Cys-428.fwdarw.Ser and Cys-429.fwdarw.Gly **modified** toxins had reduced activity on erythrocytes and **polymorphonuclear** leukocytes, being 6 and 20 times less active than the wild type, resp. However, all the **modified** toxins formed oligomers in erythrocyte membranes to the same extent as the wild-type recombinant toxin. This suggests that the cysteine residue at position 428 is involved in neither the binding of toxin to membranes nor its insertion into the membrane, and also that the formation of oligomers is not by itself sufficient for toxin activity.

L3 ANSWER 13 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1988:547401 CAPLUS
DOCUMENT NUMBER: 109:147401

TITLE: Stimulation of human neutrophils, monocytes, and platelets by **modified** C-reactive protein (CRP) expressing a neoantigenic specificity

AUTHOR(S): Potempa, L. A.; Zeller, J. M.; Fiedel, B. A.; Kinoshita, C. M.; Gewurz, H.

CORPORATE SOURCE: Dep. Immunol./Microbiol., Rush Presbyterian St. Luke's Med. Cent., Chicago, IL, USA

SOURCE: Inflammation (N. Y.) (1988), 12(4), 391-405
CODEN: INFLD4; ISSN: 0360-3997

DOCUMENT TYPE: Journal

LANGUAGE: English

AB C-reactive protein (CRP) can be structurally **modified** by heat, acid, or urea-chelation to express a neoantigen designated as neo-CRP. This antigen is also expressed on the in vitro primary protein translocation products of both human and rabbit CRP. Unmodified CRP and CRP complexed with **pneumococcal** C-polysaccharide (CPS) do not express neo-CRP. Forms of CRP expressing neo-CRP but not native CRP antigenicity (even in the presence of CPS) consistently and in a dose-dependent manner potentiated the respiratory burst response of human **polymorphonuclear** leukocytes and peripheral blood monocytes to heat-**modified** IgG. Forms of CRP expressing neo-CRP antigenicity also induced reactions of aggregation and secretion from isolated platelets and potentiated platelet activation stimulated by ADP in platelet-rich-plasma, while native CRP alone or complexed with CPS again did not. Unlike CRP-CPS complexes, forms of CRP expressing neo-CRP were not able to activate the complement system. These data emphasize the biol. potential inherent in this humoral acute-phase reactant, particularly in the activation of the formed elements of the blood important in the inflammatory response. Since these cell-activating properties are preferentially obsd. when CRP is structurally **modified** to express the neo-CRP antigen, such a mol. conversion may be central to the structure-function relationships of CRP at local sites of inflammation and tissue injury.

L3 ANSWER 14 OF 26 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1988:17214 CAPLUS

DOCUMENT NUMBER: 108:17214

TITLE: Overproduction and rapid purification of the amidase of Streptococcus pneumoniae

AUTHOR(S): Garcia, J. L.; Garcia, E.; Lopez, R.

CORPORATE SOURCE: Cent. Invest. Biol., C.S.I.C., Madrid, 28006, Spain

SOURCE: Arch. Microbiol. (1987), 149(1), 52-6
CODEN: AMICCW; ISSN: 0302-8933

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Oligonucleotide-directed **mutagenesis** of a plasmid contg. the lytA gene coding for the **pneumococcal** amidase has allowed the sepn. of the coding sequence of the gene. This sequence has been placed in plasmid pIN-III(lppP-5)-A3 downstream from both a **modified** lipoprotein promoter and the lactose promoter to construct the recombinant plasmid pGL100. When Escherichia coli RB 791 (pGL100) was grown in the presence of lactose, the **pneumococcal** amidase accounted for 7% of the total protein present in this strain after 18 h incubation at 37.degree.. The overproduced amidase was purified in a single-step procedure using a choline-Sepharose 6B column, taking advantage of the fact that this enzyme was the unique protein with affinity for choline present in exts. obtained from E. coli RB791 (pGL100). The development of the above design opens up the possibility of studying the mechanism that regulates the activity of this important autolysin by using physicochem. techniques that require the availability of high amts. of purified amidase.

L3 ANSWER 15 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1985:519684 CAPLUS
DOCUMENT NUMBER: 103:119684
TITLE: Localized conversion in Streptococcus pneumoniae recombination: heteroduplex preference
AUTHOR(S): Sicard, Michel; Lefevre, Jean Claude; Mostachfi, Pezechpour; Gasc, Anne Marie; Sarda, Claudine
CORPORATE SOURCE: Cent. Rech. Biochim. Genet. Cell., CNRS, Toulouse, 31062, Fr.
SOURCE: Genetics (1985), 110(4), 557-68
CODEN: GENTAE; ISSN: 0016-6731
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In **pneumococcal** transformation, the frequency of recombinants between point **mutations** is generally proportional to distance. An aberrant marker in the amiA locus enhanced recombination frequency when crossed with any other allele of this gene. The hyperrecombination obsd. in 2-point crosses could be explained by 2 hypotheses: the aberrant marker induces frequent crossovers in its vicinity or the **mutant** is converted to wild type. Evidence is presented to show that in suitable 3-point crosses, this hyperrecombination does not **modify** the recombination frequency between outside markers, suggesting that a conversion occurs at the site of this **mutation**. To est. the length over which this event occurs, very closely linked markers were isolated and used in 2-point crosses. It appears that the conversion system removes only a few base pairs (from 3-27) around the aberrant marker. This conversion process is quite different from the mismatch-repair system controlled by hex genes in **pneumococcus**, which involves several thousand base pairs. Moreover, artificial heteroduplexes were constructed using sepd. DNA

strands. It appears that only 1 of the 2 heteroduplexes is specifically converted. The conversion system acts upon 5'..ATTAAT..3'/3'..TAAGTA..5'. A possible role of the palindrome resulting from the **mutation** is discussed.

L3 ANSWER 16 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1985:22561 CAPLUS
DOCUMENT NUMBER: 102:22561
TITLE: Opsonic activity of immunoglobulin prepared for intravenous use
AUTHOR(S): Hetherington, Seth V.; Giebink, G. Scott
CORPORATE SOURCE: Dep. Pediatr., Albany Med. Cent., Albany, NY, 12208, USA
SOURCE: J. Lab. Clin. Med. (1984), 104(6), 977-86
CODEN: JLCMAK; ISSN: 0022-2143
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The opsonic activity of 2 Ig prepns. **modified** for i.v. infusion was tested against Streptococcus pneumoniae types 3, 7F, and 14 and 2 strains of Staphylococcus aureus by **polymorphonuclear** leukocyte uptake of [3H]thymidine-labeled bacteria. Reduced and alkylated Ig (Chem-IgG) and Ig prepd. by chromatog. with diethylaminoethyl-Sephadex (DEAE-IgG) were evaluated with and without complement and compared with the opsonic activity of immune serum globulin and heated pooled human serum. Opsonic activity of DEAE-IgG was greater than that of Chem-IgG and equiv. to the activity of immune serum globulin and pooled human serum against S. aureus 502A and type 3 **pneumococcus**. Both i.v. Igs had lower opsonic activity than either pooled human serum or immune serum globulin against type 14 **pneumococcus**. There were no differences in antibody avidity for **pneumococcal** antigen among the Igs tested. All 4 opsonins had similar opsonic activity against the protein A-deficient S. aureus Wood 46. **Modification** of Ig for i.v. infusion by chem. alteration may adversely affect opsonic activity by changing the Fc portion of the antibody mol.

L3 ANSWER 17 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1984:101355 CAPLUS
DOCUMENT NUMBER: 100:101355
TITLE: The role of C5 in **polymorphonuclear** leukocyte recruitment in response to Streptococcus pneumoniae
AUTHOR(S): Toews. Galen B.; Vial, Wayne C.
CORPORATE SOURCE: Southwestern Med. Sch., Univ. Texas, Dallas, TX, 75235, USA
SOURCE: Am. Rev. Respir. Dis. (1984), 129(1), 82-6
CODEN: ARDSBL; ISSN: 0003-0805
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Congenic complement C5-sufficient B10.D2/nSn (C5+) and C5-deficient B10.D2/oSn (C5-) mice were used to det. the importance of the C5 mol. in the **polymorphonuclear** leukocyte (PMN) response to S. pneumoniae. The C5+ and C5- mice were injected with water and varying inoculums of **pneumococci** via an endobronchial catheter. Bronchoalveolar lavage (BAL) was performed on the inoculated lung at 0 and 4 h after injection. Cellular response was measured and chemotactic activity was assayed in BAL supernatants at each time interval, using human PMN in a **modified** Boyden chamber. Clearance of bacteria was studied by a quant. lung culture. The C5+ mice recruited more PMN after challenges with both 104 and 106 **pneumococci** than did the C5- mice; however, PMN accumulation did occur in C5- mice. Similarly, C5+ mice generated more intraalveolar chemotactic activity than did C5- mice, but chemotactic activity was present in both C5+ and C5- mice, as detd. by checkerboard assays. Pulmonary clearance of bacteria was impaired in the absence of C5 at both inoculums. Thus, the C5 mol. yields important PMN chemotaxins during the early time period after intrapulmonary inoculation of S. pneumoniae. However, PMN recruitment after this insult also results from other chemotaxins since both chemotactic activity and PMN recruitment occur within the alveoli of C5- mice.

L3 ANSWER 18 OF 26 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1983:102390 CAPLUS

DOCUMENT NUMBER: 98:102390

TITLE: **Mutagenesis** in Streptococcus pneumoniae (**Pneumococcus**) by transformation with DNA **modified** by the carcinogen-**mutagen**, aflatoxin B1

AUTHOR(S): Stark, Avishay A.; Giroux, Craig N.

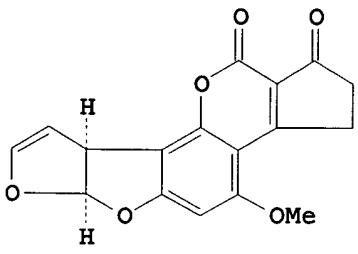
CORPORATE SOURCE: Dep. Biochem., Tel-Aviv Univ., Tel-Aviv, Israel

SOURCE: Mutat. Res. (1983), 107(1), 23-32
CODEN: MUREAV; ISSN: 0027-5107

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

Searcher : Shears 308-4994

AB Covalent binding of metabolically activated aflatoxin B1 (AFB1)(I) [1162-65-8] to transforming DNA of **Pneumococcus** caused a decrease in transforming activity and induced **mutations** to antibiotic resistance in recipients. The 2 effects were proportional, in vitro, to the covalent binding levels of AFB1 to **pneumococcal** DNA.

L3 ANSWER 19 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1975:560665 CAPLUS
DOCUMENT NUMBER: 83:160665
TITLE: **Modifier mutation** affecting utilization of mannitol in **pneumococcus**
AUTHOR(S): Rotheim, Minna B.; Hotchkiss, Rollin D.
CORPORATE SOURCE: Upstate Med. Cent., State Univ. New York, Syracuse, N. Y., USA
SOURCE: Can. J. Microbiol. (1975), 21(8), 1139-43
CODEN: CJMIAZ
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The altered growth of a **pneumococcal mutant** contg. marker M, which confers ability to utilize mannitol, and a **modifier** gene is reported. The **modifier** gene is closely linked to the M gene and imposes a requirement for growth in 0.4% glucose before growth in mannitol medium. The tentative position of the M gene of **pneumococcus** is ery-r str-r M sul-rd.

L3 ANSWER 20 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1974:548335 CAPLUS
DOCUMENT NUMBER: 81:148335
TITLE: Marker discrimination and **mutagen** induced alterations in **pneumococcal** transformation
AUTHOR(S): Tiraby, Jean G.; Fox, Maurice S.
CORPORATE SOURCE: Dep. Biol., Massachusetts Inst. Technol., Cambridge, Mass., USA
SOURCE: Genetics (1974), 77(3), 449-58
CODEN: GENTAE
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nitrous acid-induced and NH2OH-induced chem. alterations in transforming DNA resulted in the loss of biol. activity and in **mutagenesis**. The function responsible for the discrimination between high efficiency and low efficiency markers in **pneumococcal** transformation, and for the elimination of a substantial fraction of spontaneously occurring **mutational** events, did not appear to act on integrated DNA carrying these chem.

alterations. The chem. **modifications** resulted in **mutations** that were evident among bacteria transformed with the treated DNA. Fusidic acid-resistant **mutants** isolated in this way were predominantly of the low efficiency class. Most **mutations** of spontaneous origin occurring in this locus are of the high efficiency class. Discrimination probably results from the elimination of specific classes of base pair mismatches that occur as intermediates in transformation. The base pair mismatches most effectively eliminated in the discriminating strain of **pneumococcus** are probably those of the A:C and G:T type and the immediate product of transformation with **mutagenized** DNA involves intermediates that are not recognized as A:C or G:T by the discrimination system.

L3 ANSWER 21 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1974:35024 CAPLUS
DOCUMENT NUMBER: 80:35024
TITLE: Integration efficiency in DNA-induced transformation of **Pneumococcus** [Diplococcus pneumoniae]. II. Genetic studies of **mutant** integrating all the markers with a high efficiency
AUTHOR(S): Tiraby, Gerard; Sicard, Michel A.
CORPORATE SOURCE: Lab. Genet., Univ. Paul Sabatier, Toulouse, Fr.
SOURCE: Genetics (1973), 75(1), 35-48
CODEN: GENTAE
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Transformation of the D. pneumosiae **mutant** 401 by DNA's bearing a std. ref. marker and several other markers belonging to 2 unlinked loci showed that differences in the integration efficiencies of these markers were considerably reduced in this strain compared to the wild-type strain Cl3. The sensitivities of **mutant** 401 to uv light and to x-irradn. were the same as those of Cl3. However, in 401 all the markers tested were more resistant to inactivation as shown by transformation of 401 and Cl3 by uv-irradiated DNA. The increase in resistance was greater for low-efficiency (LE) markers than for high-efficiency (HE) markers. The decreased discrimination between LE and HE markers in strain 401 was not due to a mechanism related to **modification** of markers in the transforming DNA by the recipient cells, nor were the proteins inducing competence of the cells responsible for the differences in the integration efficiencies of various markers. Genetic studies of the fate of recombinants as well as the measure of the amt. of DNA taken up showed that all markers were integrated into strain 401 by the same recombination process, that specific for HE markers.

L3 ANSWER 22 OF 26 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1974:35023 CAPLUS
DOCUMENT NUMBER: 80:35023
TITLE: Integration efficiency in DNA-induced transformation of **pneumococcus** [Diplococcus pneumoniae]. I. Method of transformation in solid medium and its use for isolation of transformation-deficient and recombination-**modified mutants**
AUTHOR(S): Tiraby, Gerard; Claverys, Jean P.; Sicard, Michel A.
CORPORATE SOURCE: Lab. Genet., Univ. Paul Sabatier, Toulouse, Fr.
SOURCE: Genetics (1973), 75(1), 23-33
CODEN: GENTAE
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A method of transformation on solid medium esp. adapted for D. pneumoniae was developed. Under specific conditions, all colonies that were allowed to grow in the presence of transforming DNA gave rise to transformed bacteria. Combined with replica plating this technique was used to isolate **mutants modified** with regard to recombination. Most of the **mutants** found were transformation-defective and showed a large diversity in their response to uv light. Some of these **mutants** had lost their ability to take up transforming DNA. One **mutant** showed a reduced yield of transformants for a given quantity of DNA taken up. **Mutants** that manifest altered behavior with regard to marker efficiencies were also isolated. One of these exhibited a decrease in the transformation efficiency of only the high-efficiency markers and 2 **mutants** showed a decrease in the transformation efficiency of the low efficiency markers.

L3 ANSWER 23 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1970:9696 CAPLUS
DOCUMENT NUMBER: 72:9696
TITLE: Comparison of the x-ray sensitivities of thymidine, transforming DNA, and bacteria
AUTHOR(S): Apelgot, Sonia; Rebeyrotte, N.
CORPORATE SOURCE: Lab. Curie Pasteur, Inst. Radium, Paris, Fr.
SOURCE: Biophysik (1969), 6(1), 25-33
CODEN: BPYKAU
DOCUMENT TYPE: Journal
LANGUAGE: French

AB Thymidine-6-3H (I), transforming DNA (II) isolated from a culture of **pneumococcus** R36A Smr (a **mutant** resistant to streptomycin), Escherichia coli strain B3 thy- Smr with high radioresistance, and Diplococcus pneumoniae strain R36A Smr were irradiated. The bacteria were not very sensitive to irradn., but I and II were. The sensitivity varied with the temp. and media used during the irradn. A graph of the ratio of I decomposed when

irradiated to the value for I irradiated vs. the irradn. temp. was an upward concave curve. A graph of the ratio of the value of x-ray doses which left a 37% survival of bacteria or II irradiated at 0.degree. in saline to the dose needed with oth er exptl. conditions of temp. and media vs. the irradn. temp. was a downwa rd concave curve. The weak dependence of bacterial radiosensitivity to environmental **modifications** is a property of cells. The effect of lowering temp. seemed to be a property of the DNA, not the bacteria.

L3 ANSWER 24 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1969:458006 CAPLUS
DOCUMENT NUMBER: 71:58006
TITLE: Genetic analysis by transformation of a group of uracil requiring **mutants** of Diplococcoccus pneumoniae
AUTHOR(S): Morse, Helvise G. G.; Lerman, L. S.
CORPORATE SOURCE: Med. Center, Univ. of Colorado, Denver, Colo., USA
SOURCE: Genetics (1969), 61(1), 41-60
CODEN: GENTAE
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A no. of auxotrophic **pneumococcus mutants** were isolated from a **modified** medium. **Mutants** requiring uracil, lysine, and phenylalanine were recovered. Twelve of the 40 uracil-requiring **mutants** were used in recombination expts. The transformation yield in genetic crosses was dependent on the efficiency of transformation of the recipient **mutant**. When allowance was made for recipient variation in a recombination index, reciprocals were closely related to each other, and a linear arrangement of linked markers was possible. The comparison of long map distances with the sum of intervening short distances indicated that neg. interference was operative in regions <0.2 index unit. Reasonably good additivity among recombination indexes occurred, and was improved by correction for neg. interference.

L3 ANSWER 25 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1968:112427 CAPLUS
DOCUMENT NUMBER: 68:112427
TITLE: Role of integrity and heterogeneity of deoxyribonucleic acid molecules during genetic recombination in **pneumococcal** transformation
AUTHOR(S): Kent, Joan L.; Hotchkiss, Rollin D.
CORPORATE SOURCE: Dep. Genet., Rockefeller Inst., New York, N. Y., USA
SOURCE: Physiol. Gene Mutat. Expression, Proc. Symp.

(1966), Meeting Date 1965, 165-71
CODEN: 19PXAO
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The effect of phys. and chem. **modified** DNA mols. on genetic recombination was investigated in various **pneumococcal mutants**. A method was developed which allowed the detn. of the amt. of transformation caused by the exposure to DNA for various time intervals. For **mutants** with 1 marker (e.g., streptomycin resistance or sulfonamide resistance) a linear relation was found between the time of exposure and the amt. of transformation. The rate for any given marker was detd. by the DNA concn. Two markers were often incorporated together or linked. The 3-factor linkage group was exploited by studying the effect of chem. **modification** of the DNA on single, multiple, and complex transformant classes. The kinetic study on linkage of DNA denatured by heating and renatured by cooling showed that the helical structure of DNA was of importance in the penetration step. Denaturated DNA competed with native DNA. In further expts. the technique of subcrit. heat inactivation of a multiply marked DNA was used. The decay of transformations (assayed on a concd., wild-type culture at 3 .times. 107 viable counts/ml. exposed to 0.02 .mu.g. of **modified** DNA for 5 min. at 30.degree.) accumulated more quickly in the case of a triply marked group than in a singly marked one. Tightly linked markers, loosely linked markers, and unlike pairs were usually inactivated at the same exponential rate for a typical single marker. More interestingly, the cells seemed to be able to escape the consequences of exposure to damaged DNA. If the damaged sites were incorporated one would expect either a **mutagenic** or a lethal effect. Neither one was observed in the appropriate expts.

L3 ANSWER 26 OF 26 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1967:616 CAPLUS
DOCUMENT NUMBER: 66:616
TITLE: Interaction of **mutations** affecting growth rate and resistance to streptomycin in **pneumococci** and streptococci
AUTHOR(S): Krauss, Marjorie R.; King, James Clement; Cox, Rody P.
CORPORATE SOURCE: New York Univ. Med Center, New York, N. Y., USA
SOURCE: J. Bacteriol. (1966), 92(5), 1337-44
CODEN: JOBAAY
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A strain of Streptococcus (viridans group) was shown by transformation reactions to be the carrier of 2 interacting **mutations**. One produced resistance to streptomycin and a slow rate of growth; the only effect of the 2nd was an increase in

growth rate when it was added by transformation to streptococcal strains that had already been transformed to bear the 1st. Similar **modifying mutations** were observed in strains of streptococci and **pneumococci** into which the 1st **mutation** had been introduced by transformation. 16 references.

=> d his l4-; d 1-27 ibib abs

(FILE 'MEDLINE, BIOSIS, EMBASE, JICST-EPLUS, TOXLINE, TOXLIT, CONFSCI, PHIC, PHIN' ENTERED AT 16:04:40 ON 02 SEP 1999)
L4 80 S L3
L5 27 DUP REM L4 (53 DUPLICATES REMOVED)

L5 ANSWER 1 OF 27 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998109732 MEDLINE
DOCUMENT NUMBER: 98109732
TITLE: A conserved tryptophan in **pneumolysin** is a determinant of the characteristics of channels formed by **pneumolysin** in cells and planar lipid bilayers.
AUTHOR: Korchev Y E; Bashford C L; Pederzolli C; Pasternak C A; Morgan P J; Andrew P W; Mitchell T J
CORPORATE SOURCE: Department of Cellular and Molecular Sciences, St. George's Hospital Medical School, London, U.K.
SOURCE: BIOCHEMICAL JOURNAL, (1998 Feb 1) 329 (Pt 3) 571-7. Journal code: 9YO. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199805
ENTRY WEEK: 19980501
AB **Pneumolysin** is one of the family of thiol-activatable, cytolytic toxins. Within these toxins the amino acid sequence Trp-Glu-Trp-Trp is conserved. **Mutations** made in this region of **pneumolysin**, residues 433-436 inclusive, did not affect cell binding or the formation of toxin oligomers in the target cell membrane. However, the **mutations** did affect haemolysis, leakage of low-molecular-mass metabolites from Lettre cells and the induction of conductance channels across planar lipid bilayers. Of eight **modified pneumolysins** examined, Trp-433-->Phe showed the smallest amount of haemolysis or leakage (less than 5% of wild type). **Pneumolysin**-induced leakage from Lettre cells was sensitive to inhibition by bivalent cations but the extent of inhibition varied depending on the **modification**. Leakage by the **mutant** Trp-433-->Phe was least sensitive to cation inhibition. The ion-conducting channels formed across planar lipid bilayers exhibit small (less

than 30 pS), medium (30 pS-1 nS) and large (more than 1 nS) conductance steps. Small- and medium-sized channels were preferentially closed by bivalent cations. In contrast with wild-type toxin, which formed predominantly small channels, the **modified** toxin Trp-433-->Phe formed large channels that were insensitive to cation-induced closure. Polysaccharides of molecular mass more than 15 kDa inhibited haemolysis by wild-type toxin, but polysaccharide of up to 40 kDa did not prevent haemolysis by Trp-433-->Phe. Electron microscopy revealed that Trp-433-->Phe formed oligomeric arc and ring structures with dimensions identical with those of wild-type toxin, and that the ratio of arcs to rings formed was the same for wild-type toxin and the Trp-433-->Phe variant. We conclude that the change Trp-433-->Phe affects channel formation at a point subsequent to binding to the cell membrane and the formation of oligomers, and that the size of arc and ring structures revealed by electron microscopy does not reflect the functional state of the channels.

L5 ANSWER 2 OF 27 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1999033058 MEDLINE
DOCUMENT NUMBER: 99033058
TITLE: The molecular mechanism of **pneumolysin**, a virulence factor from Streptococcus pneumoniae.
AUTHOR: Rossjohn J; Gilbert R J; Crane D; Morgan P J; Mitchell T J; Rowe A J; Andrew P W; Paton J C; Tweten R K; Parker M W
CORPORATE SOURCE: The Ian Potter Foundation Protein Crystallography Laboratory, St. Vincent's Institute of Medical Research, 41 Victoria Parade, Fitzroy, Victoria, 3065, Australia.. jamie@brains.medstv.unimelb.edu.au
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (1998 Nov 27) 284 (2) 449-61.
Journal code: J6V. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199902
ENTRY WEEK: 19990204
AB **Pneumolysin**, a member of the thiol-activated cytolysin family of toxins, is a virulence factor from the Gram-positive bacterium Streptococcus pneumoniae. The toxin forms large oligomeric pores in cholesterol-containing membranes of eukaryotic cells. A plethora of biochemical and **mutagenesis** data have been published on **pneumolysin**, since its initial characterization in the 1930s. Here we present an homology model of the monomeric and oligomeric forms of **pneumolysin** based on the recently determined crystal structure of perfringolysin O and electron microscopy data. A feature of the model is a striking

electronegative surface on parts of **pneumolysin** that may reflect its cytosolic location in the bacterial cell. The models provide a molecular basis for understanding the effects of published **mutagenesis** and biochemical **modifications** on the toxic activity of **pneumolysin**. In addition, spectroscopic data are presented that shed new light on **pneumolysin** activity and have guided us to hypothesise a detailed model of membrane insertion. These data show that the environment of some tryptophan residues changes on insertion and/or pore formation. In particular, spectroscopic analysis of a tryptophan **mutant**, W433F, suggests it is the residue mainly responsible for the observed effects. Furthermore, there is no change in the secondary structure content when the toxin inserts into membranes. Finally, the basis of the very low activity shown by a **pneumolysin** molecule from another strain of S. pneumoniae may be due to the movements of a key domain-domain interface. The molecular basis of **pneumolysin**-induced complement activation may be related to the structural similarity of one of the domains of **pneumolysin** to Fc, rather than the presumed homology of the toxin to C-reactive protein as previously suggested. Copyright 1998 Academic Press.

L5 ANSWER 3 OF 27 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1998323373 MEDLINE
DOCUMENT NUMBER: 98323373
TITLE: Application of molecular typing to the epidemiology of Streptococcus pneumoniae.
AUTHOR: Hall L M
CORPORATE SOURCE: Department of Medical Microbiology, St Bartholomew's, London, UK.. l.m.c.hall@mds.qmw.ac.uk
SOURCE: JOURNAL OF CLINICAL PATHOLOGY, (1998 Apr) 51 (4) 270-4. Ref: 45
Journal code: HT3. ISSN: 0021-9746.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199809
ENTRY WEEK: 19980903
AB The spread of antibiotic resistance and the development of new vaccines have focused attention on the epidemiology of Streptococcus pneumoniae over recent years. While serotyping and the determination of antibiotic resistance remain primary methods for characterising **pneumococci**, molecular typing can add greater discrimination and complementary information. Methods based on restriction fragment length **polymorphism** within total DNA or non-specific

polymerase chain reaction provide information representative of the whole genome and can be used to recognise closely related isolates from different sources, whether in the investigation of possible cross infection at the local level or in the investigation of national or international spread of antibiotic resistant strains. Fingerprinting of penicillin binding protein genes adds further information in the analysis of penicillin resistant isolates. The use of a combination of typing methods to analyse both the genome as a whole and specific loci has led to the realisation that **pneumococci** undergo horizontal gene transfer much more often than most other bacterial species. In particular the spread of penicillin resistance has been characterised by a combination of the spread of epidemic strains, transfer of chromosomal resistance genes from such strains into other genetic backgrounds, and transfer of capsule genes resulting in the switch of serotypes within strains. In the future molecular typing will have an important role in discovering whether widespread vaccination leads to genetic **modification** of the **pneumococcal** population causing invasive disease.

L5 ANSWER 4 OF 27 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 4
ACCESSION NUMBER: 1997:486725 BIOSIS
DOCUMENT NUMBER: PREV199799785928
TITLE: Dissemination of antibiotic resistance.
AUTHOR(S): Roy, Paul H.
CORPORATE SOURCE: Cent. Rech. Cent. Hosp. Univ. Laval, Dep. Biochim., Univ. Laval, 2705 boulevard Laurier, Sainte-Foy, PQ G1V 4G2 Canada
SOURCE: M-S (Medecine Sciences), (1997) Vol. 13, No. 8-9, pp. 927-933.
ISSN: 0767-0974.
DOCUMENT TYPE: General Review
LANGUAGE: French
SUMMARY LANGUAGE: French; English
AB While antibiotics have, for the past fifty years, been "miracle drugs", we are presently facing the "end of the miracle". The increasing use of antibiotics has led to the selection of bacteria resistant to multiple antibiotics. Diverse mechanisms of resistance are found in resistant bacteria. Among these are enzymatic degradation or alteration of antibiotic molecules (e.g. beta-lactamases and aminoglycoside **modifying** enzymes), altered targets (e.g. penicillin-binding proteins and dihydrofolate reductase), and drug efflux (e.g. of tetracycline). Often point **mutations** can drastically alter the enzyme or the target: beta-lactamases become able to digest third-generation cephalosporins, dihydrofolate reductase becomes resistant to trimethoprim, and DNA gyrase becomes resistant to quinolones. Resistance genes have not always been present in common pathogenic bacteria, but have been evolving in antibiotic producing bacteria or

in those cohabiting with them in the environment, and have recently been acquired by horizontal transfer. Many resistance genes are on conjugative plasmids of wide host range, often as part of transposons. Examples are the TEM beta-lactamase, whose gene can **mutate** to yield resistance to third-generation cephalosporins, and vancomycin resistance in enterococci, where a complete metabolic pathway for an altered cell wall in encoded by a transposon. In addition, a novel DNA element called an integron has been described, in which individual resistance genes exist as mobile cassettes and are rearranged by site-specific recombination, in a sort of natural genetic engineering, to form strongly expressed multiresistance operons. Knowledge of the mechanisms of resistance gene evolution and dissemination and of antibiotic usage patterns leads to the prediction, in a more or less immediate future, of the emergence of vancomycin-resistant staphylococci, of multiresistant **pneumococci**, and of third-generation-cephalosporin-resistant Haemophilus and Neisseria, for which the medical community must be prepared.

L5 ANSWER 5 OF 27 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 96254545 MEDLINE
DOCUMENT NUMBER: 96254545
TITLE: In vitro activities of U-100592 and U-100766, novel oxazolidinone antibacterial agents.
AUTHOR: Zurenko G E; Yagi B H; Schaadt R D; Allison J W; Kilburn J O; Glickman S E; Hutchinson D K; Barbachyn M R; Brickner S J
CORPORATE SOURCE: Pharmacia & Upjohn, Inc., Kalamazoo, Michigan 49001, USA.
SOURCE: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (1996 Apr) 40 (4) 839-45.
Journal code: 6HK. ISSN: 0066-4804.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
AB Oxazolidinones make up a relatively new class of antimicrobial agents which possess a unique mechanism of bacterial protein synthesis inhibition. U-100592 {(S)-N-[[3-[3-fluoro-4-[4-(hydroxyacetyl)-1-piperazinyl]- phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide} and U-100766 {(S)-N-[[3-[3-fluoro-4-(4-morpholinyl)phenyl]- 2-oxo-5-oxazolidinyl]methyl]-acetamide} are novel oxazolidinone analogs from a directed chemical **modification** program. MICs were determined for a variety of bacterial clinical isolates; the respective MICs of U-100592 and U-100766 at which 90% of isolates are inhibited were as follows: methicillin-susceptible Staphylococcus aureus, 4 and 4 micrograms/ml; methicillin-resistant S. aureus, 4 and 4

micrograms/ml; methicillin-susceptible Staphylococcus epidermidis, 2 and 2 micrograms/ml; methicillin-resistant S. epidermidis, 1 and 2 micrograms/ml; Enterococcus faecalis, 2 and 4 micrograms/ml; Enterococcus faecium, 2 and 4 micrograms/ml; Streptococcus pyogenes, 1 and 2 micrograms/ml; Streptococcus pneumoniae, 0.50 and 1 microgram/ml; Corynebacterium spp., 0.50 and 0.50 micrograms/ml; Moraxella catarrhalis, 4 and 4 micrograms/ml; Listeria monocytogenes, 8 and 2 micrograms/ml; and Bacteroides fragilis, 16 and 4 micrograms/ml. Most strains of Mycobacterium tuberculosis and the gram-positive anaerobes were inhibited in the range of 0.50 to 2 micrograms/ml. Enterococcal strains resistant to vancomycin (VanA, VanB, and VanC resistance phenotypes), **pneumococcal** strains resistant to penicillin, and M. tuberculosis strains resistant to common antitubercular agents (isoniazid, streptomycin, rifampin, ethionamide, and ethambutol) were not cross-resistant to the oxazolidinones. The presence of 10, 20, and 40% pooled human serum did not affect the antibacterial activities of the oxazolidinones. Time-kill studies demonstrated a bacteriostatic effect of the analogs against staphylococci and enterococci but a bactericidal effect against streptococci. The spontaneous **mutation** frequencies of S. aureus ATCC 29213 were <3.8 x 10(-10) and <8 x 10(-11) for U-100592 and U-100766, respectively. Serial transfer of three staphylococcal and two enterococcal strains on drug gradient plates produced no evidence of rapid resistance development. Thus, these new oxazolidinone analogs demonstrated in vitro antibacterial activities against a variety of clinically important human pathogens.

L5 ANSWER 6 OF 27 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96071271 EMBASE
DOCUMENT NUMBER: 1996071271
TITLE: Bacterial resistance to carbapenems.
AUTHOR: Livermore D.M.
CORPORATE SOURCE: Department of Medical Microbiology, London Hospital Medical College, Turner Street,London E1 2AD, United Kingdom
SOURCE: Advances in Experimental Medicine and Biology, (1996) 390/- (25-48).
ISSN: 0065-2598 CODEN: AEMBAP
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The carbapenems have the broadest spectra of all .beta.-lactams but resistance still occurs, caused by target **modification**, impermeability or .beta.-lactamase production. Target **modification** or replacement is important in methicillin-

resistant staphylococci, E. faecium and some **pneumococci**. These organisms present the greatest current threat to carbapenem efficacy. Impermeability to carbapenems arises in P. aeruginosa **mutants**, where it is contingent on loss of D2 outer membrane protein, a minor porin. This resistance functions only if the Pseudomonas retains its chromosomal group 1 .beta.-lactamase, and so reflects the interplay of impermeability and hydrolysis rather than impermeability alone; nevertheless porin loss is the critical change that engenders resistance. Resistance based on impermeability coupled to a group 1 .beta.-lactamase has also been described in E. cloacae, but demands loss of a major porin and is much rarer and less stable than in P. aeruginosa. Although group 1 .beta.-lactamases contribute to resistance in these organisms, they have only feeble carbapenemase activity. Chromosomal .beta.-lactamases with potent carbapenemase activity occur in most or all X. maltophilia. A. hydrophila and F. odoratum isolates. These enzymes, which cause carbapenem resistance when expressed copiously, are all zinc-dependent. Zinc carbapenemases also are a concern in B. fragilis, where they are encoded by the chromosomal DNA of c. 3% of isolates, though expressed by only 1%. Carbapenemases are extremely rare outside these species. Nevertheless, a plasmidic zinc carbapenemase was reported from one P. aeruginosa isolate and from several S. marcescens. Further carbapenemases, some not zinc-dependent, are known from a tiny numbers of Serratia, Enterobacter, and Acinetobacter isolates. Despite these various modes of resistance, carbapenems have retained their efficacy far heller than have expanded-spectrum cephalosporins. Whether this advantage will be retained indefinitely is uncertain. If resistance does become more prevalent it may be possible to derivatize the carbapenems so as to extend their activity. There is already interest in the design of carbapenems that bind .beta.-lactam-resistant PBPs and, to an extent, in the development of carbapenemase inhibitors.

L5 ANSWER 7 OF 27 MEDLINE
ACCESSION NUMBER: 96342056 MEDLINE
DOCUMENT NUMBER: 96342056
TITLE: Bacterial resistance to carbapenems.
AUTHOR: Livermore D M
CORPORATE SOURCE: Department of Medical Microbiology, London Hospital Medical College, UK.
SOURCE: ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1995) 390 25-47. Ref: 80
Journal code: 2LU. ISSN: 0065-2598.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY WEEK: 19970104
AB The carbapenems have the broadest spectra of all beta-lactams but resistance still occurs, caused by target **modification**, impermeability or beta-lactamase production. Target **modification** or replacement is important in methicillin-resistant staphylococci, E. faecium and some **pneumococci**. These organisms present the greatest current threat to carbapenem efficacy. Impermeability to carbapenems arises in P. aeruginosa **mutants**, where it is contingent on loss of D2 outer membrane protein, a minor porin. This resistance functions only if the Pseudomonas retains its chromosomal group 1 beta-lactamase, and so reflects the interplay of impermeability and hydrolysis rather than impermeability alone; nevertheless porin loss is the critical change that engenders resistance. Resistance based on impermeability coupled to a group 1 beta-lactamase has also been described in E. cloacae, but demands loss of a major porin and is much rarer and less stable than in P. aeruginosa. Although group 1 beta-lactamases contribute to resistance in these organisms, they have only feeble carbapenemase activity. Chromosomal beta-lactamases with potent carbapenemase activity occur in most or all X. maltophilia, A. hydrophila and F. odoratum isolates. These enzymes, which cause carbapenem resistance when expressed copiously, are all zinc-dependent. Zinc carbapenemases also are a concern in B. fragilis, where they are encoded by the chromosomal DNA of c. 3% of isolates, though expressed by only 1%. Carbapenemases are extremely rare outside these species. Nevertheless, a plasmidic zinc carbapenemase was reported from one P. aeruginosa isolate and from several S. marcescens. Further carbapenemases, some not zinc-dependent, are known from a tiny numbers of Serratia, Enterobacter, and Acinetobacter isolates. Despite these various modes of resistance, carbapenems have retained their efficacy far better than have expanded-spectrum cephalosporins. Whether this advantage will be retained indefinitely is uncertain. If resistance does become more prevalent it may be possible to derivatize the carbapenems so as to extend their activity. There is already interest in the design of carbapenems that bind beta-lactam-resistant PBPs and, to an extent, in the development of carbapenemase inhibitors.

L5 ANSWER 8 OF 27 TOXLINE
ACCESSION NUMBER: 1994:52791 TOXLINE
DOCUMENT NUMBER: CRISP-94-A04008-02
TITLE: SYNTHESIS OF OLIGONUCLEOTIDES.
AUTHOR: PROBST P G
CORPORATE SOURCE: FDA
U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, SYSOUT o

CONTRACT NUMBER: Z01BA04008-02
SOURCE: (1992). Crisp Data Base National Institutes Of Health. Award Type: G = Grant
DOCUMENT TYPE: (RESEARCH)
FILE SEGMENT: CRISP
LANGUAGE: English
ENTRY MONTH: 199403

AB RPROJ/CRISP Synthesis of oligonucleotides by our laboratory in collaborative efforts with several laboratories within the Division of Bacterial Products has proven invaluable to the following research programs: A PCR approach to clone and express a potential surface antigen from Mycoplasma pneumonia, and to **modify** existing cloning vectors. Development of a method to allow for direct cloning of PCR generated products, and as templates for DNA sequencing in Mycoplasma. Completion of the nucleotide sequence analysis of mycobacterial genes encoding several immunoreactive antigens. Isolation of the **pneumococcal pneumolysin** gene from two types of genomic DNA, to produce trunicated point **mutations** of the pneumolynsin gene, and for conjugation of a single polysaccharide. Continued research in the production of selective **mutation** and amplification of bacterial toxin genes for use in examining the effect of **mutation** on toxin function. Primers were also utilized in the development of PCT protocols to rapidly detect non tuberculosos mycobacterial infections. Research in our laboratory is being conducted in the use of cloned overlapping strnads, to develop an in vitro transcription probe for allergenic screening of apple to determine and isolate the allergenic component. Studies are also continuing to include the use of oligonucleotides as tools for the creation of an epitope library.

L5 ANSWER 9 OF 27 MEDLINE
ACCESSION NUMBER: 93072694 MEDLINE
DOCUMENT NUMBER: 93072694
TITLE: **Modification** of resistance to Streptococcus pneumoniae by dietary ethanol, immunization, and murine retroviral infection.
AUTHOR: Darban H; Watson R R; Darban J R; Shahbazian L M
CORPORATE SOURCE: Department of Family and Community Medicine, University Medical Center, Tucson, Arizona.
CONTRACT NUMBER: AA08037 (NIAAA)
SOURCE: ALCOHOLISM, CLINICAL AND EXPERIMENTAL RESEARCH, (1992 Oct) 16 (5) 846-51.
Journal code: 35X. ISSN: 0145-6008.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
Searcher : Shears 308-4994

ENTRY MONTH: 199302

AB Hallmarks of the acquired immune deficiency syndrome (AIDS) are immunologic alterations, frequently associated with opportunistic infections. To study such associations, LP-BM5 murine retrovirus infection was used as a murine model of AIDS. Retrovirally infected and uninfected mice were fed a 5% (v/v) ethanol diet for 55 days and then fed a 7% v/v ethanol diet for the final 7 days to assert the role of ethanol as a cofactor in development of murine AIDS. There was a reduction in **polymorphonuclear** neutrophils count in ethanol-fed groups. Neutrophils increased in retrovirus-infected groups, except those vaccinated 10 days before challenge with live bacteria. The percentage of splenic lymphocytes in the retrovirus-infected group was reduced in comparison with controls. Survival of the mice challenged intraperitoneally with Streptococcus pneumoniae was increased by vaccination and suppressed by dietary alcohol. Retrovirus infection caused a much faster death rate after bacterial challenge than nonretrovirus infected controls. Vaccination played an important role in delaying the death rate in all treated groups. Transferring spleen cells from healthy, unimmunized mice also enabled the retrovirally infected mice to survive the bacterial infection longer. Enhancement of resistance to S. pneumoniae by vaccination and transfer of immunocompetent cells to mice immunosuppressed by retroviral infection show the potential to use immunomodulation to affect disease resistance in AIDS.

L5 ANSWER 10 OF 27 MEDLINE DUPLICATE 6

ACCESSION NUMBER: 92105031 MEDLINE

DOCUMENT NUMBER: 92105031

TITLE: Truncated forms of PspA that are secreted from Streptococcus pneumoniae and their use in functional studies and cloning of the pspA gene.

AUTHOR: Yother J; Handsome G L; Briles D E

CORPORATE SOURCE: Department of Microbiology, University of Alabama, Birmingham 35294..

CONTRACT NUMBER: AI28457 (NIAID)
AI21458 (NIAID)
HD17812 (NICHD)

SOURCE: JOURNAL OF BACTERIOLOGY, (1992 Jan) 174 (2) 610-8.
Journal code: HH3. ISSN: 0021-9193.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199204

AB Insertion-duplication **mutagenesis** was used to generate **mutants** of Streptococcus pneumoniae that produced truncated forms of PspA (**pneumococcal** surface protein A). The truncated products, representing from 20 to 80% of the complete PspA molecule, were all secreted from the cell and could be detected in

unconcentrated culture medium. Analysis of the truncated molecules showed that the antigenic variability known to be associated with PspA is located in the alpha-helical N-terminal half of the molecule. This region was also found to contain immunogenic and protection-eliciting epitopes and to define the maximum region of the molecule that is likely to be surface exposed. The apparent molecular weight variability seen for PspA molecules of different S. pneumoniae strains was localized to both the N- and C-terminal halves of the protein. Attachment of PspA to S. pneumoniae was found to require regions located carboxy to the fifth repeat unit in the C-terminal end of the molecule. From the insertion-duplication **mutants**, the complete pspA gene was cloned and expressed in Escherichia coli. Differences in apparent molecular weight were observed when the same cloned product was expressed in E. coli and S. pneumoniae, suggesting that PspA is **modified** differently in the two hosts.

L5 ANSWER 11 OF 27 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 92261297 MEDLINE
DOCUMENT NUMBER: 92261297
TITLE: Comparative efficacy of autolysin and **pneumolysin** as immunogens protecting mice against infection by Streptococcus pneumoniae.
AUTHOR: Lock R A; Hansman D; Paton J C
CORPORATE SOURCE: Department of Microbiology, Adelaide Children's Hospital, North Adelaide, South Australia.
SOURCE: MICROBIAL PATHOGENESIS, (1992 Feb) 12 (2) 137-43. Journal code: MIC. ISSN: 0882-4010.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199208
AB Previous studies on Streptococcus pneumoniae have established that the **pneumococcal** proteins autolysin (N-acetylmuramyl-L-alanine amidase) and **pneumolysin** both contribute significantly to the virulence of the organism. In the present work, autolysin and a defined toxoid derivative of **pneumolysin** were tested, individually and in combination, for efficacy in a mouse model as antigens protecting against challenge with virulent, wild-type S. pneumoniae. While each antigen alone provided significant protection, the degree of protection was not increased when the antigens were administered together. In an additional experiment, mice were challenged with a genetically-**modified** **mutant** strain of **pneumococcus** unable to express active **pneumolysin**. Pre-immunization of such mice with autolysin failed to provide any significant protection against the challenge. The results of this study suggest that the most important contribution made by autolysin to the virulence of S. pneumoniae may

be its role in mediating the release of **pneumolysin** from the **pneumococcal** cytoplasm during infection.

L5 ANSWER 12 OF 27 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 92114766 MEDLINE
DOCUMENT NUMBER: 92114766
TITLE: Complement activation and antibody binding by **pneumolysin** via a region of the toxin homologous to a human acute-phase protein.
AUTHOR: Mitchell T J; Andrew P W; Saunders F K; Smith A N; Boulnois G J
CORPORATE SOURCE: Department of Microbiology, University of Leicester, UK..
SOURCE: MOLECULAR MICROBIOLOGY, (1991 Aug) 5 (8) 1883-8. Journal code: MOM. ISSN: 0950-382X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199204
AB **Pneumolysin**, a membrane-damaging toxin, is known to activate the classical complement pathway. We have shown that 1 microgram ml-1 of **pneumolysin** can activate complement, which is a much lower level than observed previously. We have identified two distinct regions of **pneumolysin** which show homology with a contiguous sequence within acute-phase proteins, including human C-reactive protein (CRP). Site-directed **mutagenesis** of the **pneumolysin** gene was used to change residues common to **pneumolysin** and CRP. Some of the **modified** toxins had a reduced ability both to activate complement and bind antibody. We suggest that the ability of **pneumolysin** to activate complement is related to its ability to bind the Fc portion of immunoglobulin G.

L5 ANSWER 13 OF 27 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 92030189 MEDLINE
DOCUMENT NUMBER: 92030189
TITLE: **Pneumolysin** induces the salient histologic features of **pneumococcal** infection in the rat lung in vivo.
AUTHOR: Feldman C; Munro N C; Jeffery P K; Mitchell T J; Andrew P W; Boulnois G J; Guerreiro D; Rohde J A; Todd H C; Cole P J; et al
CORPORATE SOURCE: Department of Thoracic Medicine, National Heart and Lung Institute, Brompton Hospital, London, United Kingdom..
SOURCE: AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY, (1991 Nov) 5 (5) 416-23. Journal code: AOB. ISSN: 1044-1549.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199202

AB Streptococcus pneumoniae infections are common, but how they cause host tissue injury and death is incompletely understood. Immunization with **pneumolysin**, a thiol-activated toxin produced by the **pneumococcus**, partially protects animals during subsequent infection. The mechanism by which **pneumolysin** contributes to disease is not known. The aim of the present investigation was to determine the histologic changes induced by recombinant **pneumolysin** in the rat lung and to compare them with the changes induced by live organisms. Injection of either toxin (200 or 800 ng) or bacteria into the apical lobe bronchus was associated with the development of a severe lobar pneumonia restricted to the apical lobe. The changes induced by the toxin were greater at the higher concentration, and changes were most severe in those animals in which there was partial ligation of the apical lobe bronchus. The pneumonitis was less severe following injection of a **modified** toxin with decreased hemolytic activity, generated by site-directed **mutagenesis** of the cloned **pneumolysin** gene, indicating that this property of the toxin was important in generating pulmonary inflammation. There was still considerable pneumonitis after injection of a **modified** toxin with decreased capacity to activate complement.

L5 ANSWER 14 OF 27 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 89307578 MEDLINE
DOCUMENT NUMBER: 89307578
TITLE: **Pneumolysin**, the thiol-activated toxin of Streptococcus pneumoniae, does not require a thiol group for in vitro activity.
AUTHOR: Saunders F K; Mitchell T J; Walker J A; Andrew P W; Boulnois G J
CORPORATE SOURCE: Department of Microbiology, University of Leicester, United Kingdom..
SOURCE: INFECTION AND IMMUNITY, (1989 Aug) 57 (8) 2547-52. Journal code: GO7. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198910

AB The role of the single cysteine residue in the activity of the thiol-activated toxin **pneumolysin** was investigated using oligonucleotide-mediated, site-directed **mutagenesis**. Three **modified** toxins in which the cysteine residue was changed to

an alanine, a serine, or a glycine residue were purified to homogeneity and examined for activity. The Cys-428----Ala **modified** toxin was indistinguishable from the wild-type recombinant toxin in terms of hemolytic activity and lytic and inhibitory effects on human **polymorphonuclear** leukocytes (PMN), indicating that the cysteine residue is not essential for toxin activity. The Cys-428----Ser and Cys-429----Gly **modified** toxins had reduced activity on erythrocytes and **polymorphonuclear** leukocytes, being 6 and 20 times less active than the wild type, respectively. However, all the **modified** toxins formed oligomers in erythrocyte membranes to the same extent as the wild-type recombinant toxin. This suggests that the cysteine residue at position 428 is involved in neither the binding of toxin to membranes nor its insertion into the membrane, and also that the formation of oligomers is not by itself sufficient for toxin activity.

L5 ANSWER 15 OF 27 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 89007040 MEDLINE
DOCUMENT NUMBER: 89007040
TITLE: Stimulation of human neutrophils, monocytes, and platelets by **modified** C-reactive protein (CRP) expressing a neoantigenic specificity.
AUTHOR: Potempa L A; Zeller J M; Fiedel B A; Kinoshita C M; Gewurz H
CORPORATE SOURCE: Department of Immunology, Rush Presbyterian St. Luke's Medical Center, Chicago, Illinois.
CONTRACT NUMBER: R23AI23030 (NIAID)
HL-23457 (NHLBI)
HL-00614 (NHLBI)
SOURCE: INFLAMMATION, (1988 Aug) 12 (4) 391-405.
Journal code: GM0. ISSN: 0360-3997.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198901
AB C-reactive protein (CRP) can be structurally **modified** by heat, acid, or urea-chelation to express a neoantigen designated by us as neo-CRP. This antigen is also expressed on the in vitro primary protein translation products of both human and rabbit CRP. Unmodified CRP and CRP complexed with **pneumococcal** C-polysaccharide (CPS) do not express neo-CRP. Forms of CRP expressing neo-CRP but not native CRP antigenicity (even in the presence of CPS) consistently and in a dose-dependent manner potentiated the respiratory burst response of human **polymorphonuclear** leukocytes and peripheral blood monocytes to heat-**modified** IgG. Forms of CRP expressing neo-CRP antigenicity also induced reactions of aggregation and secretion

from isolated platelets and potentiated platelet activation stimulated by ADP in platelet-rich-plasma, while native CRP alone or complexed with CPS again did not. Unlike CRP-CPS complexes, forms of CRP expressing neo-CRP were not able to activate the complement system. These data emphasize the biologic potential inherent in this humoral acute-phase reactant, particularly in the activation of the formed elements of the blood important in the inflammatory response. Since these cell-activating properties are preferentially observed when CRP is structurally **modified** to express the neo-CRP antigen, such a molecular conversion may be central to the structure-function relationships of CRP at local sites of inflammation and tissue injury.

L5 ANSWER 16 OF 27 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 88105816 MEDLINE
DOCUMENT NUMBER: 88105816
TITLE: Overproduction and rapid purification of the amidase of Streptococcus pneumoniae.
AUTHOR: Garcia J L; Garcia E; Lopez R
CORPORATE SOURCE: Centro de Investigaciones Biologicas, C.S.I.C. Velazquez, Madrid, Spain..
SOURCE: ARCHIVES OF MICROBIOLOGY, (1987) 149 (1) 52-6. Journal code: 7YN. ISSN: 0302-8933.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198804
AB Oligonucleotide-directed **mutagenesis** of a plasmid containing the lytA gene coding for the **pneumococcal** amidase has allowed the separation of the coding sequence of the gene. This sequence has been placed in plasmid pIN-III(lppP-5)-A3 downstream from both a **modified** lipoprotein promoter and the lactose promoter to construct the recombinant plasmid pGL100. When Escherichia coli RB 791 (pGL100) was grown in the presence of lactose, the **pneumococcal** amidase accounted for 7% of the total protein present in this strain after 18 h incubation at 37 degrees C. The overproduced amidase was purified in a single-step procedure using a choline-Sepharose 6B column taking advantage of the fact that this enzyme was the unique protein with affinity for choline present in extracts obtained from E. coli RB791 (pGL100). The development of the above design opens up the possibility of studying the mechanism that regulates the activity of this important autolysin by using physiochemical techniques that require the availability of high amounts of purified amidase.

L5 ANSWER 17 OF 27 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 90074287 MEDLINE
DOCUMENT NUMBER: 90074287

TITLE: Gene conversion in Streptococcus pneumoniae.
AUTHOR: Sicard A M
CORPORATE SOURCE: Centre de Recherche de Biochimie et de Genetique Cellulaires du C.N.R.S., Toulouse, France..
SOURCE: MICROBIOLOGIA, (1987 Feb) 3 (1) 5-12. Ref: 57
Journal code: AIF. ISSN: 0213-4101.
PUB. COUNTRY: Spain
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199003

AB In **pneumococcus**, correction of **mutations** by the repair of mismatched bases results in gene conversion, i.e. transfer of genetic information from one strand of DNA to the other. Three different correction systems act upon a variety of **mutations** : 1) A long-patch process (a few Kb) is efficient in the elimination of transitions, mostly +/- 1 base-pair **mutations** and less efficient in eliminating some transversions without affecting fairly long deletions. Neighboring sequences may interfere with this process. It is directed by at least two genes. 2) A localized conversion system acts on a six base-pair heteroduplex structure such as 5'ATTAAT/3'TAAGTA by specifically converting the **mutated** A base to the wild type C base. **Modifications** of this configuration by site-directed **mutagenesis** lead to reduced conversion. 3) Fairly long deletions are eliminated during recombination by events that extend several scores of bases around the heterologus region. Although only the first conversion system has been shown to participate efficiently in protecting Streptococcus pneumoniae against spontaneous **mutation**, the two other processes may also eliminate **mutations** of different natures.

L5 ANSWER 18 OF 27 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 85286297 MEDLINE
DOCUMENT NUMBER: 85286297
TITLE: Localized conversion in Streptococcus pneumoniae recombination: heteroduplex preference.
AUTHOR: Sicard M; Lefevre J C; Mostachfi P; Gasc A M; Sarda C
SOURCE: GENETICS, (1985 Aug) 110 (4) 557-68.
Journal code: FNH. ISSN: 0016-6731.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198512

AB In **pneumococcal** transformation the frequency of recombinants between point **mutations** is generally

proportional to distance. We have recently described an aberrant marker in the amiA locus that appeared to enhance recombination frequency when crossed with any other allele of this gene. The hyperrecombination that we have observed in two-point crosses could be explained by two hypotheses: the aberrant marker induces frequent crossovers in its vicinity or the **mutant** is converted to wild type. In this report we present evidence showing that, in suitable three-point crosses, this hyperrecombination does not **modify** the recombination frequency between outside markers, suggesting that a conversion occurs at the site of this **mutation**. To estimate the length over which this event occurs, we isolated very closely linked markers and used them in two-point crosses. It appears that the conversion system removes only a few base pairs (from three to 27) around the aberrant marker. This conversion process is quite different from the mismatch-repair system controlled by hex genes in **pneumococcus**, which involves several thousand base pairs. Moreover, we have constructed artificial heteroduplexes using separated DNA strands. It appears that only one of the two heteroduplexes is specifically converted. The conversion system acts upon 5'..ATTAAT..3'/3'.. TAAGTA..5'. A possible role of the palindrome resulting from the **mutation** is discussed.

L5 ANSWER 19 OF 27 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 85056632 MEDLINE
DOCUMENT NUMBER: 85056632
TITLE: Opsonic activity of immunoglobulin prepared for intravenous use.
AUTHOR: Hetherington S V; Giebink G S
CONTRACT NUMBER: AI-08821 (NIAID)
SOURCE: JOURNAL OF LABORATORY AND CLINICAL MEDICINE, (1984 Dec) 104 (6) 977-86.
Journal code: IVR. ISSN: 0022-2143.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198503
AB The opsonic activity of two immunoglobulin preparations **modified** for intravenous infusion was tested against Streptococcus pneumoniae types 3, 7F, and 14 and two strains of Staphylococcus aureus by **polymorphonuclear** leukocyte uptake of 3H-thymidine-labeled bacteria. Reduced and alkylated immunoglobulin (Chem-IgG) and immunoglobulin prepared by chromatography with diethylaminoethyl-Sephadex (DEAE-IgG) were evaluated with and without complement and compared with the opsonic activity of immune serum globulin and heated pooled human serum. Opsonic activity of DEAE-IgG was greater than that of Chem-IgG and equivalent to the activity of immune serum globulin and pooled human

serum against S. aureus 502A and type 3 **pneumococcus**. Both intravenous immunoglobulins had lower opsonic activity than either pooled human serum or immune serum globulin against type 14 **pneumococcus**. There were no differences in antibody avidity for **pneumococcal** antigen among the immunoglobulins tested. All four opsonins had similar opsonic activity against the protein A-deficient S. aureus Wood 46. **Modification** of immunoglobulin for intravenous infusion by chemical alteration may adversely affect opsonic activity by changing the Fc portion of the antibody molecule.

L5 ANSWER 20 OF 27 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 84152108 MEDLINE
DOCUMENT NUMBER: 84152108
TITLE: Early pulmonary granulocyte recruitment in response to Streptococcus pneumoniae.
AUTHOR: Vial W C; Toews G B; Pierce A K
CONTRACT NUMBER: HL-21817 (NHLBI)
SOURCE: AMERICAN REVIEW OF RESPIRATORY DISEASE, (1984 Jan) 129 (1) 87-91.
Journal code: 426. ISSN: 0003-0805.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198406

AB Although **polymorphonuclear** leukocytes (PMN) are a conspicuous histologic feature of clinical and experimental **pneumococcal** pneumonia, neither the mechanism nor the magnitude of recruitment of these cells to the lung following lesser **pneumococcal** challenge is known. We have, therefore, investigated the early process of recruitment of PMN to alveolar spaces after pulmonary inoculation of Streptococcus pneumoniae in doses less than those causing pneumonia. We injected Balb/c mice with water and varying inoculums of **pneumococci** via an endobronchial catheter. Bronchoalveolar lavage (BAL) was performed on the inoculated lung at 0, 2, or 4 h after injection. Cellular response was measured and chemotactic activity was assayed on BAL supernatants at each time interval using the migration of human PMN through 3-micron filters in **modified** Boyden chambers by the leading front techniques. The BAL of normal and control animals (inoculum of sterile water only used for the control animals) yielded 5.03 +/- 1.51 X 10(2) and 0.17 +/- 0.04 X 10(5) PMN, respectively. The PMN recruitment at 4 h as a function of **pneumococcal** inoculum was described by the following equation: log PMN = 0.751 log Pn + 1.119 (r2 = 0.82, p less than 0.001). The PMN were, therefore, recruited in a dose-dependent manner. That recruitment may be caused by chemotactic substance(s) was suggested by the significant correlation between the PMN

response and the distance of in vitro migration: log PMN = 0.057 micron + 0.52 (r = 0.77, p less than 0.005). We have defined quantitatively the recruitment of PMN to the lung after **pneumococcal** challenge.(ABSTRACT TRUNCATED AT 250 WORDS)

L5 ANSWER 21 OF 27 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 84152107 MEDLINE
DOCUMENT NUMBER: 84152107
TITLE: The role of C5 in **polymorphonuclear** leukocyte recruitment in response to Streptococcus pneumoniae.
AUTHOR: Toews G B; Vial W C
SOURCE: AMERICAN REVIEW OF RESPIRATORY DISEASE, (1984 Jan) 129 (1) 82-6.
Journal code: 426. ISSN: 0003-0805.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198406

AB **Polymorphonuclear** leukocytes (PMN) play an important functional role in early pulmonary clearance of Streptococcus pneumoniae. The factors responsible for PMN recruitment to the lung after challenges with this organism are poorly defined. We used congenic C5-sufficient B10.D2/nSn (C5+) and C5-deficient B10.D2/oSn (C5-) mice to determine the importance of the C5 molecule in the PMN response to S. pneumoniae. The C5+ and C5- mice were injected with water and varying inoculums of **pneumococci** via an endobronchial catheter. Bronchoalveolar lavage (BAL) was performed on the inoculated lung at 0 and at 4 h after injection. Cellular response was measured and chemotactic activity was assayed in BAL supernatants at each time interval using human PMN in **modified** Boyden chambers by the leading front technique. Clearance of bacteria was studied by quantitative lung culture. The C5+ mice recruited significantly more PMN after challenges with both 10(4) and 10(6) **pneumococci** than did the C5- mice (p less than 0.05), but significant PMN accumulation did occur in C5- mice. Similarly, C5+ mice generated significantly more intraalveolar chemotactic activity than did C5- mice (p less than 0.05) but chemotactic activity was present in both C5+ and C5- mice in checkerboard assays. Pulmonary clearance of bacteria was significantly impaired in the absence of C5 at both inoculums (p less than 0.05). Our results indicate that the C5 molecule yields important PMN chemotaxins during the early time period after intrapulmonary inoculation of S. pneumoniae. However, PMN recruitment after this insult also results from other chemotaxins because both chemotactic activity and PMN recruitment occur within the alveoli of C5- mice.

Searcher : Shears 308-4994

L5 ANSWER 22 OF 27 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 83257856 MEDLINE
DOCUMENT NUMBER: 83257856
TITLE: [Kinetics of the local immune response in lobar pneumonia].
Cinetique de la reponse immunitaire locale dans les pneumonies lobaires.
AUTHOR: Lafitte J J; Steenhouwer F; Roussel M; Courcol R; Voisin C; Caillaux M; Debosker Y; Geslin P
SOURCE: BULLETIN EUROPEEN DE PHYSIOPATHOLOGIE RESPIRATOIRE, (1983 Mar-Apr) 19 (2) 209-13.
Journal code: BGX. ISSN: 0395-3890.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198311
AB In 19 patients suffering from lobar pneumonia and treated with antibiotics, bronchoalveolar lavages were performed in attempt to follow the course of the biological disorders caused by the pulmonary bacterial infection. The cytologic study of the fluid harvested from 14 patients with normal immune reactivity showed, firstly, a **polymorphonuclear** leucocytosis and, after about ten days, a lymphocytosis, reaching 30 to 70% of the alveolar cell population. These cell disorders existed only in the lobe affected by the pneumonia process. In five alcoholics (one of them also splenectomized), the **polymorphonuclear** leucocytosis lasted 15 to 25 days and the lymphocytosis was delayed and moderate. We also searched for the **pneumococcal** antigen by counter-current immunoelectrophoresis using a polyvalent antiserum. We found it in 13 patients, 7 with a positive hemoculture for **pneumococcus** and 6 negatives. Clearance of this antigen was slow, non **modified** by alcoholism. We found this antigen in two patients later, between the 90th and 110th days, in the lavage fluid concentrated fifty times. The quantitative and qualitative study of the immunoglobulins revealed considerable individual variations, owing to the variable intensity of the local inflammation phenomenons and to the technical difficulties of their dosage in the lavage fluid.

L5 ANSWER 23 OF 27 MEDLINE DUPLICATE 19
ACCESSION NUMBER: 83141533 MEDLINE
DOCUMENT NUMBER: 83141533
TITLE: **Mutagenesis** in Streptococcus pneumoniae (**pneumococcus**) by transformation with DNA **modified** by the carcinogen-**mutagen**, aflatoxin B1.
AUTHOR: Stark A A; Giroux C N
SOURCE: MUTATION RESEARCH, (1983 Jan) 107 (1) 23-32.
Searcher : Shears 308-4994

Journal code: NNA. ISSN: 0027-5107.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198306

L5 ANSWER 24 OF 27 MEDLINE DUPLICATE 20
ACCESSION NUMBER: 76020435 MEDLINE
DOCUMENT NUMBER: 76020435
TITLE: A **modifier mutation** affecting utilization of mannitol in **pneumococcus**.
AUTHOR: Rotheim M B; Hotchkiss R D
SOURCE: CANADIAN JOURNAL OF MICROBIOLOGY, (1975 Aug) 21 (8) 1139-43.
Journal code: CJ3. ISSN: 0008-4166.
PUB. COUNTRY: Canada
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197602
AB The altered growth of a **pneumococcal mutant** containing marker M, which confers ability to utilize mannitol, and a **modifier** gene is reported. The **modifier** gene is closely linked to the M gene and imposes a requirement for growth in 0.4% glucose before growth in mannitol medium. The tentative position of the M gene of **pneumococcus** is ery-r str-r M sul-rd.

L5 ANSWER 25 OF 27 MEDLINE DUPLICATE 21
ACCESSION NUMBER: 74054088 MEDLINE
DOCUMENT NUMBER: 74054088
TITLE: Integration efficiency in DNA-induced transformation of **Pneumococcus**. I. A method of transformation in solid medium and its use for isolation of transformation-deficient and recombination-**modified mutants**.
AUTHOR: Tiraby G; Claverys J P; Sicard M A
SOURCE: GENETICS, (1973 Sep) 75 (1) 23-33.
Journal code: FNH. ISSN: 0016-6731.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
ENTRY MONTH: 197403

L5 ANSWER 26 OF 27 TOXLINE
ACCESSION NUMBER: 1991:40582 TOXLINE
DOCUMENT NUMBER: EMIC-16357
TITLE: INTEGRATION EFFICIENCY IN DNA-INDUCED TRANSFORMATION

OF **PNEUMOCOCCUS**. 1.A METHOD OF TRANSFORMATION IN SOLID MEDIUM AND ITS USE FOR ISOLATION OF TRANSFORMATION DEFICIENT AND RECOMBINATION **MODIFIED MUTANTS**.
AUTHOR: TIRABY G; CLAVERYS J; SICARD M A
SOURCE: GENETICS, (1973). Vol. 75, pp. 23-33.
CODEN: GENTAE.
DOCUMENT TYPE: (ORIGINAL DATA)
FILE SEGMENT: EMIC
LANGUAGE: Unavailable
ENTRY MONTH: 199103

L5 ANSWER 27 OF 27 MEDLINE
ACCESSION NUMBER: 69161419 MEDLINE
DOCUMENT NUMBER: 69161419
TITLE: [Bacteria **modified** by parietal alteration. Streptococci, staphylococci, **pneumococci**; their frequency in hemocultures. Attempted interpretation].
Les bacteries **modifiees** par alteration de la paroi. Streptocoques, Staphylocoques, Pneumocoques; leur frequence dans les hemocultures. Essai d'interpretation.
AUTHOR: Nativelle R; Deparis M
SOURCE: PRESSE MEDICALE, (1968 Nov 27) 76 (46) 2199-200.
Journal code: PLP. ISSN: 0032-7867.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196907

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L6 1 SEA ABB=ON PLU=ON PNVJ1 OR PNVJ20 OR PNVJ22 OR PNVJ45 OR PNVJ56 OR PNV103 OR PNV207 OR PNV111 OR PNV21 OR PNVJ(W)(1 OR 20 OR 22 OR 45 OR 56) OR PNV(W)(103 OR 207 OR 111 OR 211)
L7 0 SEA ABB=ON PLU=ON L6 NOT L3

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L8 0 SEA ABB=ON PLU=ON L6

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Named poly-peptides claims 7-15